

What is claimed is:

1. An in vitro method of predicting the association of a test agent with zone 3 necrosis, comprising:

- a) determining the level of expression of each of the genes listed in Table 5 in a cell exposed to said test agent;
- b) comparing said level of expression to the level of expression of said genes in a control population exposed to at least one control agent;
- c) identifying a statistically significant alteration in the level of expression in the presence of the test agent

wherein, if present, said alteration indicates that said test agent is predicted to be toxic.

2. The method of claim 1, wherein said level of expression is determined by detecting a gene transcript.

3. An in vitro method of predicting the association of a test agent with zone 3 necrosis, comprising:

- a) determining the level of expression of each of TOXMARKER 42, 59, 65, 66, 71, 76, and 97 in a cell exposed to said test agent;
- b) comparing said level of expression to the level of expression of said genes in a control population exposed to at least one control agent;
- c) identifying a statistically significant alteration in the level of expression in the presence of the test agent

wherein, if present, said alteration indicates that said test agent is predicted to be toxic.

4. The method of claim 3, wherein said level of expression is determined by detecting a gene transcript.
5. An *in vitro* method for the prediction of the association of a test agent with zone 3 necrosis, comprising:
  - a) contacting a cell with a test agent;
  - b) evaluating the level of expression of at least five TOXMARKER genes listed on Table 5
  - c) comparing said level of expression of those genes recited in step (b) to the level of expression of said genes in a control population exposed to at least one control agent;
  - d) identifying from the comparison in step (c) an statistically significant alteration at a p-value of least 0.05, in expression levels of said TOXMARKER genes in the presence of the test agent, wherein said alteration indicates that said agent is predicted to be toxic.
6. The method of claim 5, wherein said level of expression is determined by detecting a gene transcript.
7. An *in vivo* method of predicting the association of a test agent with zone 3 necrosis, comprising:
  - a) providing a cell from a subject exposed to said test agent
  - b) determining the level of expression of each of the TOXMARKER 42, 59, 65, 66, 71, 76, and 97 in said cell;
  - c) comparing said level of expression to the level of expression of said genes in a control population exposed to at least one control agent;

d) identifying a statistically significant alteration in the level of expression in the presence of the test agent

wherein, if present, said alteration indicates that said test agent is predicted to be toxic.

8. The method of claim 7, wherein said level of expression is determined by detecting a gene transcript.

9. A method for screening for changes in gene expression associated with a toxic agent, comprising:

a) determining the level of expression of each of the genes listed in Table 5 in a cell exposed to a test agent;

b) comparing said level of expression to the level of expression of said genes in a control population exposed to at least one control agent;

c) identifying a statistically significant alteration in the level of expression in the presence of the test agent

thereby screening for changes in gene expression associated with a toxic agent.

10. A zone 3 necrosis reference expression profile, comprising:

a) a pattern of gene expression of two or more genes selected from the group consisting of the genes listed on Table 3 and 5 or

b) a pattern of gene expression of TOXMARKER 42, 59, 65, 66, 71, 76, and 97.

11. An array comprising of plurality of oligonucleotides which binds

a) the nucleic acid sequences of TOXMARKER 1-132;

b) the nucleic acid sequences of the genes listed on Table 5

c) the nucleic acid sequences of TOXMARKER 42, 59, 65, 66, 71, 76, and 97;  
or

d) the nucleic acid sequences of at least five TOXMARKER genes listed on Table 5, wherein said genes identify a hepatotoxic agent with a confidence level of a p-value of least 0.05.